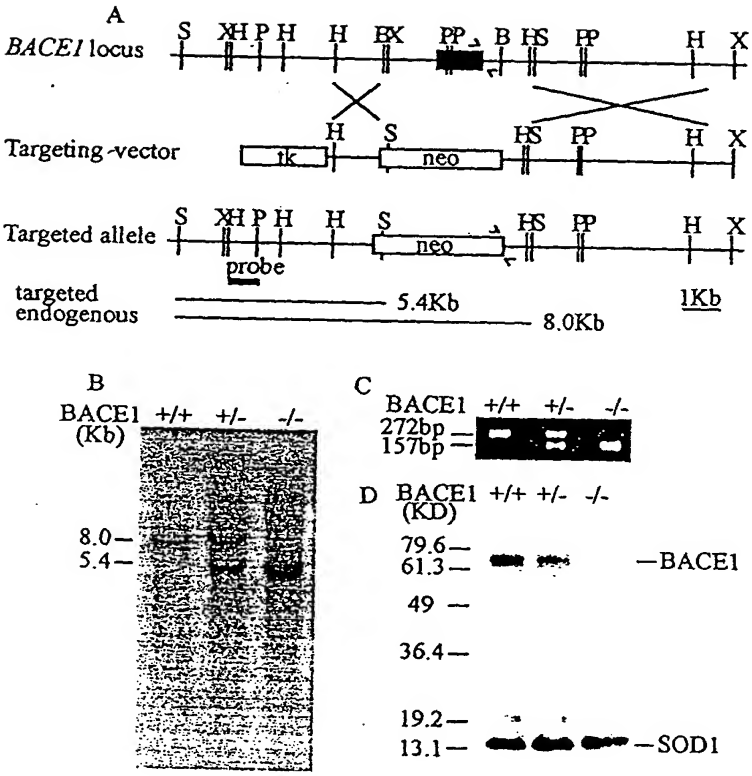

A
BACE1 locus
S XH P H H BX PP B HS PP H X
Targeting vector
H S HS PP H X
tk
neo
Targeted allele
S XH P H H S HS PP H X
neo
probe
targeted
endogenous
5.4Kb
8.0Kb
1Kb
B
BACE1 +/+ +/- -/-
(Kb)
8.0
5.4
C
BACE1 +/+ +/- -/-
272bp
157bp
D BACE1 +/+ +/- -/-
(KD)
79.6
61.3
49
36.4
19.2
13.1
—BACE1
—SOD1

FIGURE 1

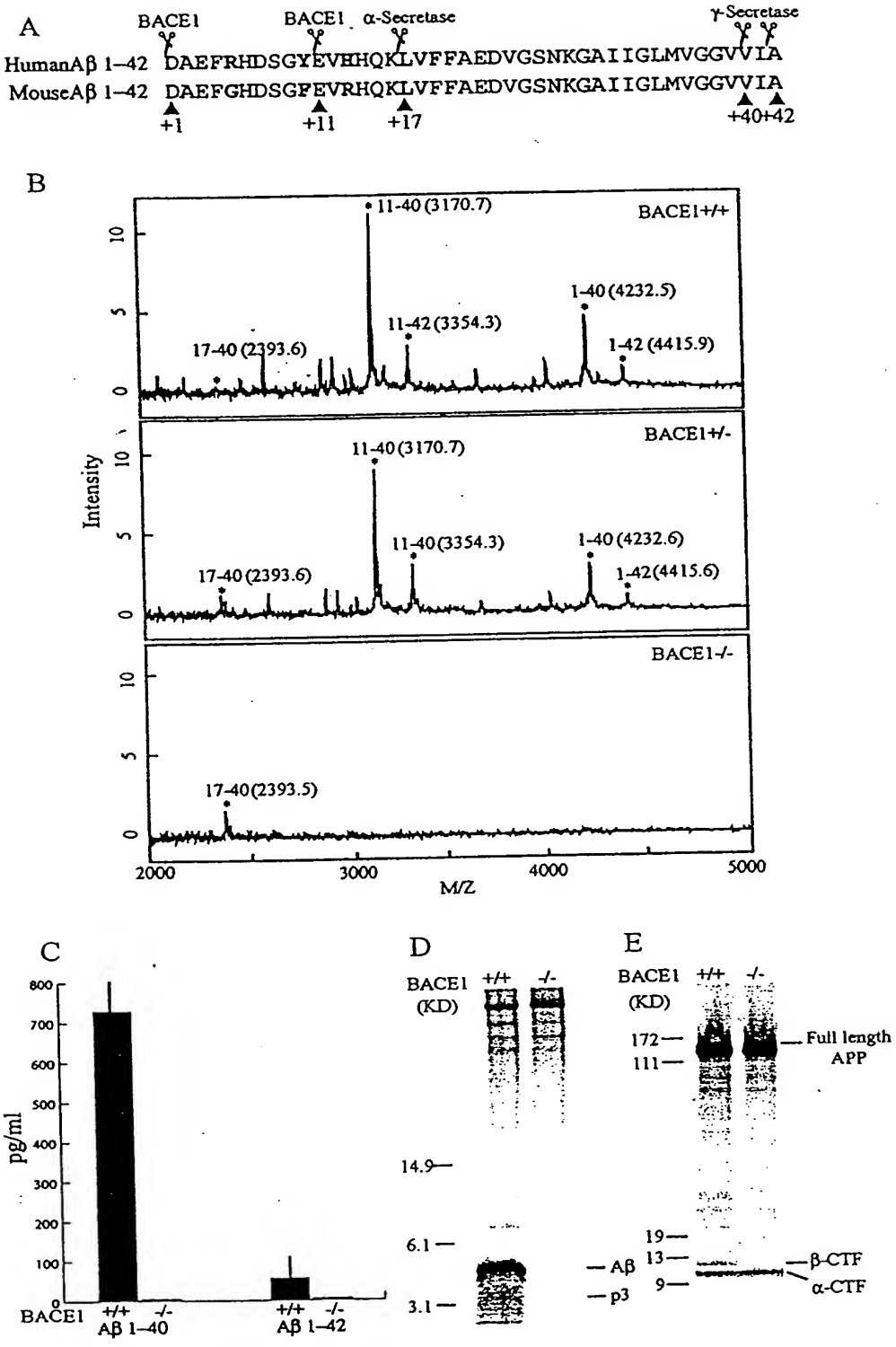
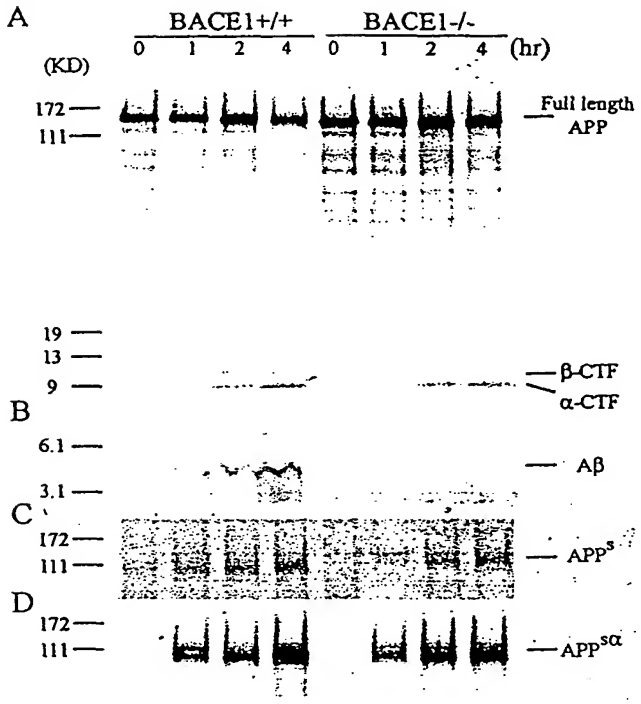

A
BACE1
BACE1
α-Secretase
γ-Secretase
HumanAβ 1–42 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA
MouseAβ 1–42 DAEFGHDSGFEVRHQKLVFFAEDVGSNKGAIIGLMVGGVVIA
+1
+11
+17
+40+42
B
BACE1+/+
11-40 (3170.7)
1-40 (4232.5)
11-42 (3354.3)
17-40 (2393.6)
1-42 (4415.9)
BACE1+/-
11-40 (3170.7)
11-40 (3354.3)
1-40 (4232.6)
17-40 (2393.6)
1-42(4415.6)
BACE1-/-
17-40(2393.5)
Intensity
M/Z
2000
3000
4000
5000
C
pg/ml
BACE1 +/+ -/- +/+ -/-
Aβ 1–40
Aβ 1–42
D
BACE1 (KD)
+/+ -/-
14.9
6.1
3.1
E
BACE1 (KD)
+/+ -/-
172
111
Full length APP
19
13
9
Aβ
p3
β-CTF
α-CTF

FIGURE 2


A
BACE1+/+
BACE1-/-
0 1 2 4 0 1 2 4 (hr)
(KD)
172
111
Full length APP
19
13
9
β-CTF
α-CTF
B
6.1
Aβ
3.1
C
172
111
APP^s
D
172
111
APP^sα

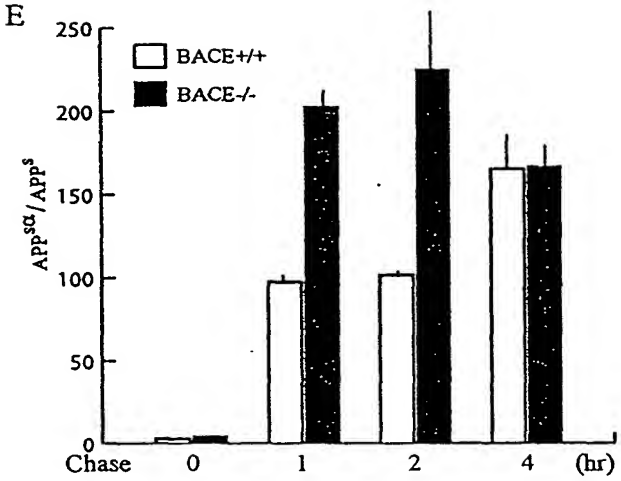

E
250
200
150
100
50
0
BACE+/+
BACE-/-
APP^sα/APP^s
Chase 0 1 2 4 (hr)

FIGURE 3